Andersen-Tawil syndrome

Anderson-Tawil syndrome is a disorder that causes episodes of muscle weakness (periodic paralysis), changes in heart rhythm (arrhythmia), and developmental abnormalities. The most common changes affecting the heart are ventricular arrhythmia, which is a disruption in the rhythm of the heart's lower chambers, and long QT syndrome. Long QT syndrome is a heart condition that causes the heart (cardiac) muscle to take longer than usual to recharge between beats. If untreated, the irregular heartbeats can lead to discomfort, fainting (syncope), or cardiac arrest.

Physical abnormalities associated with Andersen-Tawil syndrome typically affect the head, face, and limbs. These features often include a very small lower jaw (micrognathia), dental abnormalities, low-set ears, widely spaced eyes, and unusual curving of the fingers or toes (clinodactyly). Some affected people also have short stature and an abnormal curvature of the spine (scoliosis).

Two types of Andersen-Tawil syndrome are distinguished by their genetic causes. Type 1, which accounts for about 60 percent of all cases of the disorder, is caused by mutations in the *KCNJ2* gene. The remaining 40 percent of cases are designated as type 2; the cause of these cases is unknown.

Frequency

Andersen-Tawil syndrome is a rare genetic disorder; its incidence is unknown. About 100 people with this condition have been reported worldwide.

Genetic Changes

Mutations in the *KCNJ2* gene cause Andersen-Tawil syndrome.

The *KCNJ2* gene provides instructions for making a protein that forms a channel across cell membranes. This channel transports positively charged atoms (ions) of potassium into muscle cells. The movement of potassium ions through these channels is critical for maintaining the normal functions of muscles used for movement (skeletal muscles) and cardiac muscle. Mutations in the *KCNJ2* gene alter the usual structure and function of potassium channels or prevent the channels from being inserted correctly into the cell membrane. Many mutations prevent a molecule called PIP2 from binding to the channels and effectively regulating their activity. These changes disrupt the flow of potassium ions in skeletal and cardiac muscle, leading to the periodic paralysis and irregular heart rhythm characteristic of Andersen-Tawil syndrome.

Researchers have not determined the role of the *KCNJ2* gene in bone development, and it is not known how mutations in the gene lead to the developmental abnormalities often found in Andersen-Tawil syndrome.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, a person with Andersen-Tawil syndrome inherits the mutation from one affected parent. Other cases result from new mutations in the *KCNJ2* gene. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- Andersen cardiodysrhythmic periodic paralysis
- Andersen syndrome
- ATS
- Long QT syndrome 7
- LQT7
- Periodic paralysis, potassium-sensitive cardiodysrhythmic type

Diagnosis & Management

These resources address the diagnosis or management of Andersen-Tawil syndrome:

- GeneReview: Andersen-Tawil Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1264
- Genetic Testing Registry: Andersen Tawil syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1563715/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Arrhythmias
  https://medlineplus.gov/ency/article/001101.htm
- Health Topic: Arrhythmia
  https://medlineplus.gov/arrhythmia.html
- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html

Genetic and Rare Diseases Information Center

- Andersen-Tawil syndrome
  https://rarediseases.info.nih.gov/diseases/9453/andersen-tawil-syndrome

Additional NIH Resources

- National Heart, Lung, and Blood Institute
  https://www.nhlbi.nih.gov/health/health-topics/topics/qt/

Educational Resources

- Centre for Genetics Education (Australia)
  http://www.genetics.edu.au/Publications-and-Resources/Genetics-Fact-Sheets/FS58PRIMARYARRYTHMOGENICDISORDERS.pdf
- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/long-qt-syndrome
- Disease InfoSearch: Andersen Tawil Syndrome
  http://www.diseaseinfosearch.org/Andersen+Tawil+Syndrome/431
- KidsHealth from the Nemours Foundation
  http://kidshealth.org/en/teens/arrhythmias.html
- MalaCards: andersen syndrome
  http://www.malacards.org/card/andersen_syndrome
- Merck Manual Home Edition for Patients and Caregivers: Long QT Syndrome
  http://www.merckmanuals.com/home/heart-and-blood-vessel-disorders/abnormal-heart-rhythms/long-qt-syndrome-and-torsades-de-pointes-ventricular-tachycardia
- Orphanet: Cardiodysrhythmic potassium-sensitive periodic paralysis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=37553

Patient Support and Advocacy Resources

- American Heart Association
  http://www.heart.org/
- Muscular Dystrophy Association
  https://www.mda.org/disease/inherited-and-endocrine-myopathies
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/conghart.html
- Sudden Arrhythmia Death Syndromes (SADS) Foundation: Long QT Syndrome
  http://www.sads.org/What-is-SADS/Long-QT-Syndrome#.Vds6vpdGdD8

GeneReviews

- Andersen-Tawil Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1264

Genetic Testing Registry

- Andersen Tawil syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1563715/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Andersen-Tawil+syndrome%22+OR+%22Long+QT+Syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28andersen-tawil+syndrome%5BTI%5D%29+OR+%28andersen+syndrome%5BTI%5D%29+OR+%28andersen's+syndrome%5BTI%5D%29%29+OR+%28lqt7%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- ANDERSEN CARDIODYSRHYTHMIC PERIODIC PARALYSIS
  http://omim.org/entry/170390

Sources for This Summary

- Bendahhou S, Fournier E, Sternberg D, Bassez G, Furby A, Sereni C, Donaldson MR, Larroque MM, Fontaine B, Barhanin J. In vivo and in vitro functional characterization of Andersen's syndrome mutations. J Physiol. 2005 Jun 15;565(Pt 3):731-41. Epub 2005 Apr 14.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15831539
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1464553/
- Davies NP, Imbrici P, Fialho D, Herd C, Bilsland LG, Weber A, Mueller R, Hilton-Jones D, Ealing J, Boothman BR, Giunti P, Parsons LM, Thomas M, Manzur AY, Jurkat-Rott K, Lehmann-Horn F, Chinnery PF, Rose M, Kullmann DM, Hanna MG. Andersen-Tawil syndrome: new potassium channel mutations and possible phenotypic variation. Neurology. 2005 Oct 11;65(7):1083-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16217063
- Donaldson MR, Jensen JL, Tristani-Firouzi M, Tawil R, Bendahhou S, Suarez WA, Cobo AM, Poza JJ, Behr E, Wagstaff J, Szepetowski P, Pereira S, Mozaffar T, Escolar DM, Fu YH, Ptácek LJ. PIP2 binding residues of Kir2.1 are common targets of mutations causing Andersen syndrome. Neurology. 2003 Jun 10;60(11):1811-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12796536
- Donaldson MR, Yoon G, Fu YH, Ptacek LJ. Andersen-Tawil syndrome: a model of clinical variability, pleiotropy, and genetic heterogeneity. Ann Med. 2004;36 Suppl 1:92-7. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15176430
- GeneReview: Andersen-Tawil Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1264
- Modell SM, Lehmann MH. The long QT syndrome family of cardiac ion channelopathies: a HuGE review. Genet Med. 2006 Mar;8(3):143-55. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16540748
- Plaster NM, Tawil R, Tristani-Firouzi M, Canún S, Bendahhou S, Tsunoda A, Donaldson MR, Iannaccone ST, Brunt E, Barohn R, Clark J, Deymeer F, George AL Jr, Fish FA, Hahn A, Nitu A, Ozdemir C, Serdaroglu P, Subramony SH, Wolfe G, Fu YH, Ptácek LJ. Mutations in Kir2.1 cause the developmental and episodic electrical phenotypes of Andersen's syndrome. Cell. 2001 May 18; 105(4):511-9.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11371347
- Tristani-Firouzi M, Jensen JL, Donaldson MR, Sansone V, Meola G, Hahn A, Bendahhou S, Kwiecinski H, Fidzianska A, Plaster N, Fu YH, Ptacek LJ, Tawil R. Functional and clinical characterization of KCNJ2 mutations associated with LQT7 (Andersen syndrome). J Clin Invest. 2002 Aug;110(3):381-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12163457
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC151085/
- Venance SL, Cannon SC, Fialho D, Fontaine B, Hanna MG, Ptacek LJ, Tristani-Firouzi M, Tawil R, Griggs RC; CINCH investigators. The primary periodic paralyses: diagnosis, pathogenesis and treatment. Brain. 2006 Jan;129(Pt 1):8-17. Epub 2005 Sep 29. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16195244

Reviewed: April 2006
Published: February 14, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services